

GLOSSARY OF TECHNICAL TERMS

This glossary of technical terms contains explanations of certain terms used in this document as they relate to our Company and as they are used in this document in connection with our business or us. These terms and their given meanings may not correspond to standard industry definitions.

“AAV”	adeno-associated virus, which has emerged as an attractive vector for gene therapy to promote sustained gene expression in a variety of tissues such as muscle, eye, brain, liver, and lung
“AAV2”	adeno-associated virus serotype 2
“AAV8”	adeno-associated virus serotype 8
“AE”	adverse event, any unfavorable or unintended sign, symptom, disease, or abnormal lab finding that occurs during treatment or a study, regardless of whether it’s linked to the treatment in medical research and drug use.
“Aflibercept”	a humanized recombinant fusion protein which is a soluble decoy receptor that binds vascular endothelial growth factor A and B, and placental growth factor with a greater affinity than the body’s native receptors. It is called a decoy receptor since VEGF does not bind to its original receptors and mistakenly binds with aflibercept, thereby reducing VEGF activity
“AMD”	age-related macular degeneration, a degenerative retinal disease that causes progressive loss of central vision, and the leading cause of irreversible blindness in aged people
“Ang2”	Angiopoietin-2, a signaling protein crucial for blood vessel formation (angiogenesis) and responsive to growth factors like VEGF to sprout new ones, and is implicated in various diseases like cancer and retinal disorders. It’s important in conditions like diabetic macular edema (DME) and age-related macular degeneration (AMD) by promoting vascular leakage and new vessel growth.
“AOC”	antibody-oligonucleotide conjugates, belong to a class of chimeric molecules combining in their structure two important families of biomolecules: monoclonal antibodies and oligonucleotides.
“anti-VEGF”	a medicine that slows or stops the damage caused by the abnormal growth of blood vessels through blocking the VEGF protein
“ASO”	antisense oligonucleotide, a short, synthetic strand of DNA or RNA designed to bind to specific messenger RNA (mRNA) to control protein production

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“BCVA”	best corrected visual acuity, the sharpest vision someone can achieve with glasses or contacts, crucial in eye exams and clinical trials.
“BLA”	the Biologics License Application (生物製品許可申請), a request to the regulatory authorities, such as FDA or NMPA for permission to introduce, or deliver for introduction, a biologic product into interstate commerce
“CDE”	the Center for Drug Evaluation (國家藥品監督管理局藥品審評中心), a department of the NMPA responsible for evaluating drug clinical trial applications, drug marketing authorization applications, supplementary applications, and overseas production drug re-registration applications
“CDMO”	contract development and manufacturing organization, a company that serves other companies in the pharmaceutical industry on a contract basis, providing drug development and drug manufacturing services
“CHOP-INTEND”	Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders, a reliable measure of motor skills in patients with SMA-I and neuromuscular disorders presenting in infancy.
“cGMP”	current good manufacturing practices, regulations enforced by regulatory authorities such as the U.S. Food and Drug Administration, the World Health Organization, and the European Medicines Agency to ensure that pharmaceutical products, medical devices, and food products are consistently produced and controlled according to strict quality standards
“CMC”	chemistry, manufacturing, and controls processes in the development, licensure, manufacturing, and ongoing marketing of pharmaceutical products
“CNS”	central nervous system, the body’s main command center, comprising the brain and the spinal cord, responsible for processing information, integrating sensory input, and generating motor output to control all bodily functions.
“CRO(s)”	contract research organization(s), a company that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis
“CRT”	Central Retinal Thickness, a key measurement of the retina’s thickness in its central area, typically around the fovea, taken using Optical Coherence Tomography (OCT) to diagnose, monitor, and assess treatment effectiveness for eye conditions like diabetic macular edema (DME) and age-related macular degeneration (AMD).

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“DBL”	database lock, the critical process of finalizing the data by stopping all data entry and modifications, ensuring it’s complete, clean, and validated, so it’s ready for unblinding and statistical analysis to determine study outcomes and regulatory submission.
“DLT”	dose limiting toxicity, a clinically significant adverse event or abnormal laboratory value assessed as unrelated to disease progression, intercurrent illness, or concomitant medications and meeting the US National Cancer Institute common terminology criteria that are Common Terminology Criteria for Adverse Events Grade 3 (severe) or 4 (life-threatening)
“DMD”	Duchenne muscular dystrophy, a progressive, genetic (X-linked recessive) neuromuscular disorder caused by mutations to the <i>DMD</i> gene, resulting in the dysfunction or absence of the dystrophin protein.
“DME”	diabetic macular edema, a serious complication of diabetes where high blood sugar damages retinal blood vessels, causing fluid to leak into the macula.
“dose-escalation”	a process used in early-phase clinical trials, particularly Phase I studies, to identify the maximum tolerated dose of an investigational treatment
“DRG”	dorsal root ganglion, a cluster of sensory neuron cell bodies located on the dorsal (back) root of spinal nerves, acting as a crucial relay station for transmitting touch, pain, temperature, and proprioception signals from the body to the central nervous system (spinal cord and brain).
“dose-limiting toxicity”	side effects of a drug or other treatment that are serious enough to prevent an increase in dose or level of that treatment
“ETDRS letters”	A standardized tool for measuring visual acuity in eye exams
“FDA”	The United States Food and Drug Administration, a federal agency of the Department of Health and Human Services
“first-line”	the initial, preferred, or standard therapy given for a specific disease or condition, chosen for its high effectiveness and generally lower risk
“FND”	fundus neovascularization diseases, blinding eye conditions caused by abnormal growth of fragile new blood vessels in the retina. These leaky vessels lead to bleeding, fluid buildup, retinal detachment, and vision loss. The process is driven by excess vascular endothelial growth factor (VEGF), with anti-VEGF therapies being the primary treatment.

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“Gb3”	Globotriaosylceramide (Gb3, GL-3), a glycosphingolipid (a type of fat in cell membranes) that’s vital for cell function but, when it builds up, causes Fabry disease, damaging cells in blood vessels, kidneys, heart, and nervous system.
“GCP”	good clinical practice, an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the engagement of human participants
“gene therapy”	medical technology that aims to produce a therapeutic effect through the manipulation of gene expression or through altering the biological properties of living cells
“ILM”	Inner limiting membrane, a crucial structural boundary between the eye’s vitreous humor and the retina, acting as a significant obstacle (barrier) to the delivery of advanced therapies like gene therapies, nanoparticles, and stem cells into the deeper retinal layers, despite being permeable to small molecules; overcoming this barrier is key for effective retinal treatments.
“IND”	investigational new drug or investigational new drug application, also known as clinical trial application in China
“IVT”	intravitreal injection a medical procedure in which medication is delivered directly into the vitreous humor, the clear gel-like substance that fills the space between the lens and the retina of the eye. This method of administration allows for targeted treatment of various eye conditions, such as age-related macular degeneration, diabetic macular edema, and retinal vein occlusion
“investigator-initiated trial” or “IIT”	investigator-initiated trial, a clinical trial in which the investigator conceives the research, develops the protocol
“in Vitro”	latin for “within the glass”, referring to studies that are performed with cells or biological molecules outside their normal biological context
“in Vivo”	latin for “within the living”, referring to studies in which the effects of various entities are tested on whole, living organisms or cells, usually animals, including humans, and plants
“MAPT”	microtubule associated protein Tau, encoding tau protein, crucial for microtubule stability in neurons, but mutations are linked to neurodegenerative diseases like Alzheimer’s disease.

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“MeCP2”	Methyl-CpG-binding protein 2, a crucial protein encoded by the <i>MECP2</i> gene, essential for normal brain development and function, acting as an epigenetic regulator that controls gene activity, especially in neurons, by binding to methylated DNA and influencing chromatin structure.
“nAMD”	neovascular AMD, a severe form of macular degeneration where abnormal, leaky blood vessels grow under the retina, causing swelling, bleeding, scarring, and rapid central vision loss, making it a major cause of blindness
“NDA”	new drug application
“NIH”	the National Institutes of Health, a part of the U.S. Department of Health and Human Services, which is the nation’s medical research agency making important discoveries that improve health and save lives
“NMPA”	the National Medical Products Administration (國家藥品監督管理局), which is in charge of comprehensive supervision on the safety management of food, health and cosmetics and is the competent authority of drug regulation in China, formerly known as China Food and Drug Administration (“CFDA”) (國家食品藥品監督管理局)
“OCT”	optical coherence tomography, a non-invasive diagnostic technique that renders an in vivo cross-sectional view of the retina
“open-label”	a trial where both the study participants and the healthcare providers know which treatment (experimental drug, existing treatment, or placebo) is being given, which is also called nonblinded
“Orphan Drug Designation”	a status given to certain drugs called orphan drugs, which show promise in the treatment, prevention, or diagnosis of orphan diseases
“Phase I clinical trial”	a study that tests the safety of a new drug candidate
“Phase II clinical trial”	a study that tests the new drug candidate on a larger group of participants, to gather information about whether and how well it works
“Phase III clinical trial”	a study for a new drug candidate that has already passed Phases I and II, which tests the new drug candidate in larger groups of participants and compares the new drug candidate against an existing treatment or a placebo to see if it works better in practice and if it has important side effects

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“PlGF”	placental growth factor, is a protein crucial for blood vessel formation angiogenesis especially in the placenta during pregnancy. In addition PlGF is also involved in various diseases, such as in the development of fundus neovascularization
“protein engineering”	the deliberate modification of amino acids in a protein, typically utilizing the known three-dimensional structure and biochemical mechanisms of the protein, often through techniques such as site-directed mutagenesis to enhance properties like stability and activity
“rAAV”	recombinant adeno-associated virus, a small, non-pathogenic viral vector that has become the leading platform for in vivo gene therapy and a modified, gene-carrying version of the AAV
“R&D”	Research and development (R&D) refers to the systematic activities taken by companies to innovate and create new products or improve existing ones, often requiring significant investment and time.
“RNAi”	RNA interference, a biological process in which RNA molecules are involved in sequence-specific suppression of gene expression by double-stranded RNA, through translational or transcriptional repression.
“RPE”	retinal pigment epithelium, a critical, single layer of pigmented cells beneath the retina, forming a vital barrier and support system for the photoreceptors (light-sensing cells) by transporting nutrients
“RP2D”	recommended Phase II dose, the specific dose and schedule of a new drug that is determined to be the most appropriate to carry forward into larger Phase 2 clinical trials.
“RVO”	retinal vein occlusion, a blockage in a retinal vein, causing blood and fluid to leak into the retina, leading to sudden, painless vision loss or blurriness in one eye. RVO is driven by increased Vascular Endothelial Growth Factor (VEGF) leakage from damaged vessels.
“SAE”	serious adverse event, any medical occurrence in human drug trials that at any dose: results in death; is life-threatening; requires inpatient hospitalization or causes prolongation of existing hospitalization; results in persistent or significant disability/incapacity; may have caused a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage
“SCS”	Suprachoroidal injection, a medical procedure used to deliver medication into the suprachoroidal space of the eye, which is a potential space between the sclera (the white outer layer) and the choroid (a vascular layer).

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“SMA”	Spinal Muscular Atrophy (SMA), a genetic neuromuscular disorder causing progressive weakness and wasting of voluntary muscles due to the death of motor neurons in the spinal cord, impacting movement, breathing, and swallowing.
“SMN”	survival motor neuron protein, encoded by the SMN1 gene, is crucial for maintaining motor neurons, the nerve cells that control muscle movement, by helping process messenger RNA (mRNA) and build essential cellular machinery for nerve growth (axons/dendrites).
“SR” or “SubR”	Subretinal injection, a precise ophthalmic surgical technique that delivers medications, gene therapy vectors, or cells directly into the subretinal space, the area between the light-sensitive retina and the underlying retinal pigment epithelium (RPE).
“vascular permeability”	the ability of blood vessels to allow the passage of plasma proteins and other macromolecules into surrounding tissues. It is a process significantly influenced by factors such as vascular endothelial growth factor
“Vector”	Vehicle, either viral or non-viral, used as microscopic delivery trucks to carry therapeutic genetic material (like a working gene) into a patient’s cells, replacing or correcting faulty DNA to treat genetic diseases, cancers, and other conditions
“VEGF”	Vascular Endothelial Growth Factor, a crucial signaling protein that stimulates the growth of new blood vessels (angiogenesis) and lymphatic vessels, vital for normal development, wound healing, and reproduction, but also involved in diseases like cancer and fundus neovascularization disorders where excessive growth is harmful.
“VEGF-A”	a biochemical signal protein that promotes angiogenesis throughout the body and in the eye. By decreasing VEGF-A activation of its native receptors, aflibercept reduces subsequent growth of new blood vessels
“VEGF-B”	a growth factor involved in blood vessel support, tissue protection, and neuronal survival, with roles beyond simple blood vessel formation (angiogenesis), acting as a crucial antioxidant to combat oxidative stress in diseases like heart disease, glaucoma, and Parkinson’s
“VEGFR”	vascular endothelial growth factor receptor, a family of receptor tyrosine kinases (VEGFR-1, -2, -3) on cell surfaces that bind VEGF, initiating signals for blood vessel growth
“wAMD”	Wet Age-Related Macular Degeneration, a serious form of AMD where abnormal, leaky blood vessels grow under the retina, causing fluid and blood leakage that rapidly damages the macula, leading to severe central vision loss.